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MARSCHEL, A

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DATE MAILED: 06/02/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3/3/92 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449. (2 sheets)
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 14, 26, 29, 40, 41, and 44-60 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 1-13, 15-25, 27, 28, 30-39, 42, and 43 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 14, 26, 29, 40, 41, and 44-60 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Applicants' arguments filed 3/3/92 have been fully considered but they are not deemed to be persuasive with regard to all of the rejections previously applied. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

The Examiner wishes to clarify the terms "diagnosis" and "prognosis" as being applied herein to avoid any confusion. By "diagnosis" the Examiner relies on the art defined practice whereby diagnosis means the use of an assay for the identification of a disease versus another disease versus a determination of a healthy individual. By "prognosis" the Examiner means the prediction or evaluation of the time course of a disease after it has been identified.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification as originally filed, does not provide support for the invention as is now claimed.

In claims 26 and 41, parts 2) and 3) of each claim, the phrases "contacting the tissue sample with a DNA segment" and "inspecting the tissue sample...", respectively, are given

without their being disclosed in the specification as filed. It is thus NEW MATTER. The specification as filed discloses only hybridization after extraction of nucleic acid from a tissue sample. Claim 29 contains NEW MATTER via its dependence from claim 26.

The practice of "classifying those patients..." as given in the last three lines of claim 44 is NEW MATTER not disclosed in the specification as filed. Claims 45-47 contain NEW MATTER due to their dependence from claim 44.

The phrase "screening patients to determine disease status" as given in claim 48, first two lines, is NEW MATTER that is not disclosed in the specification as filed. The phrase "disease status" is broader in scope than the "disease free survival" cited on page 28, last 5 lines. Claims 49-53 contain NEW MATTER via their dependence from claim 48.

In claim 54, lines 1 and 2, the phrase "determining the prognosis in patients suffering from cancer" contains NEW MATTER because the scope of this phrase is broader than the scope of the only "prognostic" determination that the Examiner has found in the specification as filed as given on page 28. Specifically, on page 28, last 5 lines, "disease free survival" is disclosed but this is far narrower in scope than the practice of "prognosis in patients" as given in claim 54. Claims 55-59 contain NEW MATTER via their dependence from claim 54.

Claims 26, 29, 41, and 44-59 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the

objection to the specification. This is a new ground of rejection but is necessitated by the amendments filed 7/3/90, 9/6/91, and 11/6/91 as papers Numbered 13, 20, and 22, respectively.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 14, 40, and 60 are rejected under 35 U.S.C. § 101 because they lack utility due to a lack of evidence supporting the cancer diagnostic utility as claimed. This rejection was previously applied in the office action mailed 12/3/91 as being based on a lack of both diagnostic as well as prognostic utility. As discussed below, the lack of diagnostic utility is being maintained as a basis for this rejection but the rejection over a lack of prognostic utility is hereby withdrawn as a rejection applied against claims including prognosis within their scope.

Applicants argue that the references listed in the argument filed 3/3/92 clearly show data that support the claimed diagnostic and prognostic utility. Each of these references are discussed as follows:

Paik et al. (1990) J. of Clinical Oncology 8(1):103-112.

This reference discloses a study of erbB-2 protein overexpression in cancers as discussed in the abstract. In lines 7-12 of the abstract tumor cells were analyzed as to the percentage indicating overexpression or overall survival

probability. Thus no correlation as to cancer versus non-cancer diagnostic evidence is therein disclosed. All of the samples analyzed already were cancerous. Thus whether erbB-2 overexpression correlates with cancer is not answered or even studied by the analysis therein disclosed. Similarly, the data in Table 1 on page 109, for example, analyzes what percentage of tumor patients show overexpression, again no diagnostic evidence, only a study of cancer after the fact. Therefore this reference supplies evidence only for the use of the instant invention for a survival prediction for patients with cancer.

King et al. (1989) Cancer Research 49:4185-4191.

Similar to the above reference this reference correlates erbB-2 overexpression to survival as evidenced by the last line of the abstract which is: "The clear amplification of the erbB-2 gene may be associated with a significantly shorter time of treatment failure.". This is not evidence of diagnostic utility.

Park et al. (1989) Cancer Research 49:6605-6609.

Park et al. studies the amplification of erbB-2 in tumors but does not study or supply evidence that erbB-2 detection is diagnostic via amplification or overexpression for cancer. For example, Figure 3 on page 6607 shows data comparing normal placental expression with various tumor samples. This comparison with only one control lacks any significant sample size for correlation that is minimally needed for verification of diagnostic utility. Clearly the reference is directed to the study of already diagnosed tumors wherein gene structure

aberration is being studied, not whether erbB-2 is diagnostic of cancer.

King et al. (1990) Seminars in Cancer Biology 1:320\9-337.

This reference supplies evidence as summarized in the abstract that "Overexpression of...erbB-2 gene has been identified in human cancers derived from a variety of tissues.". For example, Table 1 on page 330 gives overexpression and gene amplification data for various cancer cell lines but no evidence of diagnostic utility. Similarly, Table 3 shows only tumor data. What about data from the same number of normal individuals? Such evidence is missing.

Lacroix et al. (1989) Oncogene 4:145-151.

The abstract of Lacroix et al. summarizes the comparison of erbB-2 gene amplification and overexpression for a large number of tumor samples. The last line of the abstract relates erbB-2 protein levels with enhanced malignancy. None of this is evidence that erbB-2 is diagnostic of cancer. Rather it is data that documents erbB-2 amplification and overexpression as detectable in tumors. Can these effects be detected in normal tissue samples?

In summary the arguments of applicants are not persuasive to overcome the rejection based on a lack of evidence for the diagnostic utility of the instant invention. The references however do supply evidence that the instant invention does have prognostic utility, especially with regard to either patient survival or the severity of tumor malignancy. Therefore this

rejection based on 35 U.S.C. § 101 is maintained only with regard to a lack of evidence with regard to diagnostic utility. Once a tumor is diagnosed, prognostic utility is supplied by the instant invention.

The disclosure is objected to because of the following informalities:

On page 4, the word "complimentary" appears to be misspelled.

On page 5, lines 18-20, the Brief description of Figure 1 includes the statement that "detection" is shown therein. It is noted that Figure 1 does not show any such detection.

On page 6, starting at line 16, the Brief description of Figure 2 includes a restriction map. No such restriction map is shown in Figure 2.

On page 9a, the Brief description of Figure 5 lacks a description of parts A and B which are shown in Figure 5.

On page 9a, lines 13 and 18, reference is made to Figure 1B, probes a and b, respectively, whereas there is no such probes shown in Figure 1, nor is there a Figure 1B.

On page 19, line 8, a Figure 1A is cited whereas there is no Figure 1A in the instant application.

On page 20, lines 5 and 8, a Figure 1B and 1A, respectively, is cited whereas there is no Figure 1A nor 1B in the instant application.

On page 28, line 20, the word "boservations" is misspelled.

Appropriate correction is required.

Claims 14, 26, 29, 40, 41, and 44-60 are allowable over the prior art of record.

No claim is allowed.

Applicant's amendments necessitated the new grounds of rejection as summarized in the above rejections based on NEW MATTER. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).
The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

AM

A. MARSCHEL:am

May 29, 1992

M. Moskowitz 6/1/92
MARGARET MOSKOWITZ
SUPERVISORY PATENT EXAMINER
GROUP 180